I. AMENDMENTS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1 – 55. (Canceled).

- 56. (Currently Amended) A method for inhibiting the proliferation of a hyperproliferative neoplastic cell that endogenously overexpresses thymidylate synthase, comprising contacting the cell with a compound of claim 62 or a <u>5'-monophosphate</u> metabolite thereof formed after administration to a subject.
- 57. (Currently Amended) A method for treating a pathology characterized by hyperproliferative neoplastic cells that endogenously overexpresses thymidylate synthase in a subject comprising administering to the subject a compound of claim 62 or a 5'-monophosphate metabolite thereof formed after administration to a subject.
 - 58. (Canceled).
- 59. (Previously Presented) The method of claim 56 or 57, wherein Q has the formula:

60. (Previously Presented) The method of claim 56 or 57, wherein R_1 is a halogen.

- 61. (Previously Presented) The method of claim 56 or 57, wherein R_1 is of the formula $(-CH=CH)_n-R_4$, wherein n is an integer from 1 to 10, and R_4 is selected from the group consisting of H; hydroxyl; a halogen; -NHCHO; -OCN; -SCN; -N₃; -NH₂; -NHOH; -NHNH₂ and a C_2 to C_4 carbon-containing substituent selected from the group consisting of alkyl, alkenyl, alkynyl, -O-alkyl, -O-aryl, O-heteroaryl, -S-alkyl, -S-aryl, -S-heteroaryl, -NH-alkyl, -N(alkyl)₂ and NHO-alkyl.
 - 62. (Currently Amended) A compound of the formula:

wherein:

R¹ is of the formula:

$$\left\{ \frac{}{----} \left(R^2 \right) \frac{}{n} \left(R^3 \right) \frac{}{m} R^4 \right\}$$

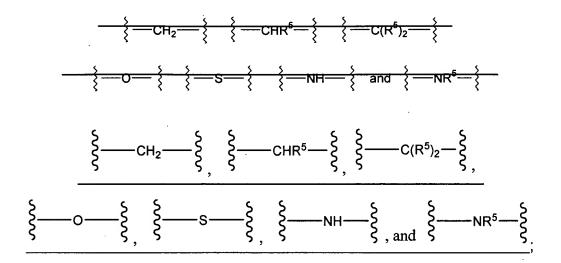
wherein R² is one of:

an unsaturated C₂ to C₄ hydrocarbyl group;

an aromatic C₄-X hydrocarbyl group, wherein X is the heteroatom; or a heteroaromatic group having the structure:

wherein J is -O-, -S-, -Se-, -NH-, or -NR^{ALK}-, wherein R^{ALK} is a linear or branched alkyl having 1 to 10 carbon atoms or a cycloalkyl group having 3 to 10 carbon atoms;

R³ is selected from the group consisting of:



wherein R⁵ may be the same or different and is independently a linear or branched alkyl group having from 1 to 10 carbon atoms, or a cycloalkyl group having from 3 to 10 carbon atoms;

wherein n is an integer from 1 to 10;

wherein m is 0 or 1;

wherein R⁴ is a toxophore selected from the group consisting of:

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wherein X is -Cl, -Br, -I, or other halogen, with the proviso that when R⁷ is -H, and

M is zero m is zero, then R⁴ is not a halogen or when m is zero and n is zero, then R⁴ is not a halogen;

wherein Y is independently -H or -F;

wherein Z is independently -O- or -S-;

wherein Q is selected from the group consisting of:

$$R^7-O$$
 R^7-O
 R^7-

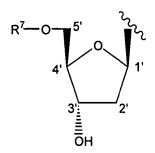
$$R^7$$
— C^2 — O
 R^6
 R^6
 R^6
 R^6
 R^6
 R^6

wherein R^6 is independently -H, -OH, -OC(=O)CH₃, or -O-Rg wherein Rg $\underline{}$ O-Rg wherein Rg is a hydroxyl protecting group other than acetyl; and,

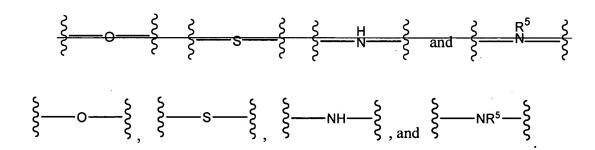
wherein R⁷ is hydrogen or a phosphoramidatyl derivative of a naturallyecurring occurring amino acid;

and wherein said compound may be in any enantiomeric, diasteriomeric, or stereoisomeric form, consisting of a D-form, L-form, α -anomeric form, and β -anomeric form.

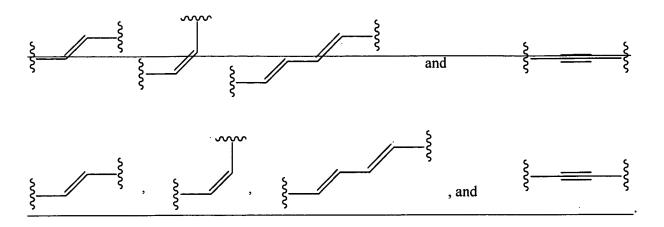
63. (Original) A compound according to claim 62, wherein Q is:



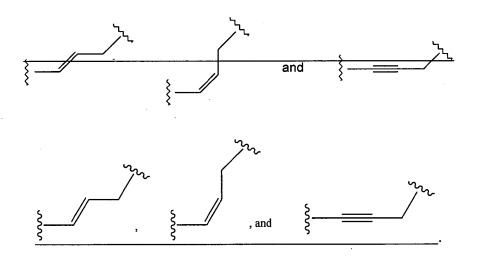
64. (Currently Amended) A compound of claim 62, wherein R³ is selected from the group consisting of:



65. (Currently Amended) A compound of claim 62, wherein R² is selected from the group consisting of:



66. (Currently Amended) A compound of claim 62, wherein R² and R³, taken together form a structure selected from the group consisting of:



- 67. (Canceled).
- 68. (Canceled).
- 69. (Previously Presented) A compound of claim 62, wherein R⁷ is:

70. (Previously presented) A compound of claim 62, wherein R⁷ is:

- 71. (Canceled).
- 72. (Canceled).
- 73. (Original) A compound of claim 62, wherein R⁴ is selected from the group consisting of:

74. (Original) A compound of claim 62, wherein R⁴ is selected from the group consisting of:

$$\left\{ \begin{array}{ccc} O & & \\ & &$$

75. (Original) A compound of claim 62, wherein R⁴ is:

76. (Currently Amended) A compound of claim 62, wherein R⁴ is:

$$\begin{array}{c} \text{CH}_{3} \\ \downarrow \\ \text{C} = \text{O} \\ \downarrow \\ \text{NH} \quad \text{OH} \\ \downarrow \quad \downarrow \\ \xi - \text{Z} - \text{CH}_{2} - \text{CH} - \text{CH} - \text{CH} = \text{CH} - (\text{CH}_{2})_{12} \text{CH}_{3} \end{array}$$

77. (Currently Amended) A compound of claim 62, wherein R⁴ is:

$$\begin{array}{c} \bullet \\ \parallel \\ \hline \\ --Z-CF_2-CH_2-CHF-C-OH \end{array}$$

$$\begin{array}{c} & & \text{O} \\ & \parallel \\ \hline \\ --\text{Z}-\text{CF}_2-\text{CHF}-\text{CH}_2-\text{C}-\text{OH} \end{array}$$

$$\underbrace{\left\{ -z-cF_2-cH_2-c-oH\right\}}_{\bullet}$$
 or

$$\left.\begin{array}{cccc} & & \text{CH}_3 & \text{O} \\ & & \parallel & \parallel \\ --\text{Z}-\text{CF}_2-\text{CH}--\text{C}-\text{OH} \end{array}\right.$$

78. (Original) A compound of claim 62, wherein R⁴ is:

$$\left\{ --Z-CF_2- \begin{matrix} Y \\ C-Y \end{matrix} \right.$$

79. (Original) A compound of claim 62, wherein R⁴ is:

$$-$$
 Z--CF₂--CH₂--CH₂-NO₂

- 80. (Canceled).
- 81. (Canceled).
- 82. (Canceled).
- 83. (Canceled).
- 84. (Canceled).
- 85. (Canceled).
- 86. (Canceled).

- 87. (Canceled).
- 88. (Currently Amended) The method of claims <u>56 or 57</u> <u>86 or 87</u>, wherein the hyperproliferative cell is a cancer cell.
- 89. (Original) The method of claim 88, wherein the cancer cell is selected from the group consisting of a colorectal cell, a head and neck cancer cell, a breast cancer cell, a liver cancer cell and a gastric cancer cell.